10/036568 Box Seq 1646

TRANSMITTAL LETTER (General - Patent Pending)	Docket No. 11373

In Re Application Of: **Tracy A. Willson, et al.**

New Serial # 10,036,568

Serial No.	Filing Date	Examiner	Group Art Unit
~~09/081,843~~	**June 29, 1998**	**Nirmal Singh Basi**	**1646**

Title:

A NOVEL HAEMOPOIETIN RECEPTOR AND GENETIC SEQUENCES ENCODING SAME

TO THE COMMISSIONER FOR PATENTS:

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PRELIMINARY AMENDMENT
STATEMENT UNDER 37 C.F.R. 1.821(F)
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in th above identified application.

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Dated: **July 7, 2003**

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Tracy A. Willson, et al.	**Examiner**:	Unassigned
Serial No:	10/036,568	**Art Unit**:	1646
Filed:	November 7, 2001	**Docket**:	11373Z
For:	A NOVEL HAEMOPOIETIN RECEPTOR AND GENETIC SEQUENCES ENCODING SAME	**Date**:	July 7, 2003

6/B
M.G.J
7/28/03

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Sir:

Applicants submit the following amendment for entry in the above-identified case.

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

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Dated: July 7, 2003

Peter I. Bernstein

IN THE SPECIFICATION:

Page 31, beginning at line 10, please amend the paragraph to read as follows:

~~BRIEF DESCRIPTION OF THE FIGURES~~ BRIEF DESCRIPTION OF THE DRAWINGS

~~Figure 1 is a representation of~~ Figures 1A-1F show the nucleotide ([SEQ ID NO:1]) and predicted amino ([SEQ ID NO:2]) sequence of murine NR4. The untranslated region is shown in lower case and the translated region in upper case. The conventional one-letter code for amino acids is employed, potential asparagine linked glycosylation sites are underlined and the conserved cysteine residues and WSXWS (SEQ ID NO: 9) motif of haempoietin receptor family members are shown in bold. The predicted signal sequence is underlined in bold while the transmembrane domain is underlined with dashes. The sequence shown is a composite derived from the analysis of 8 cDNA clones derived from 3 libraries. The 5'-end of the sequence (nucleotides –60 to 351) is derived from a single cDNA clone but is also present in genomic DNA clones that have been isolated. Boxed region – typical haempoietin receptor domain, amino acids 118-340.

B1

Page 31, beginning at line 27, please amend the paragraph to read as follows:

~~Figure 3 is a graphical representation depicted~~ Figures 3A-3B depict saturation isotherms of ^{125}I-IL-13 and ^{125}I-IL-4 binding; saturation isotherms depicted as Scatchard plots of IL-4(°) and IL-13(•) binding to ~~(A)~~ COS cells expressing the IL-13Rα(NR4) (Figure 3A), ~~(B)~~ CTLL cells (Figure 3B) and ~~(C)~~ CTLL cells expressing the IL-13Rα(NR4) (Figure 3C). Data have been normalized to 1 x10^4 COS cells and 1x10^6 CTLL cells and binding was carried out on ice for 2 to 4 hours.

B2

Page 32, beginning at line 3, please amend the paragraph to read as follows:

~~Figure 4 is a graphical representation showing~~ Figures 4A-4D show specificity of IL-4 and IL-13 binding; the ability of IL-4(°) and IL-13(•) to compete for ^{125}I-IL-13 binding to ~~(A)~~ COS cells expressing the IL-13Rα(NR4) (Figure 4A) and ~~(C)~~ CTLL cells expressing the IL-13Rα (NR4) (Figure 4C) or to compete for ^{125}I-IL-4 binding to ~~(B)~~ CTLL cells (Figure 4) and ~~(D)~~ CTLL cells expressing the IL-13Rα(NR4) (Figure 4). Binding was carried out a 4°C for 2 to 4 hours and the data expressed as a percentage of the specific binding observed in the absence of a competitor (▵).

Page 32, beginning at line 10, please amend the paragraph to read as follows:

~~Figure 5 is a graphical representation showing~~ Figures 5A-5B show factor dependent proliferation of cells expressing NR4. Two hundred ~~(A)~~ CTLL cells (Figure 5) or ~~(B)~~ CTLL cells (Figure 5) expressing the IL-13Rα (NR4) were incubated in the absence of cytokine or with various concentrations of IL-2 (□), IL-4(°) or IL-13 (•). After 48 hours viable cells were counted and data were expressed as a percentage of the number of viable cells observed with a maximal concentration of IL-2.

Page 32, beginning at line 3, please amend the paragraph to read as follows:

~~Figure 7 is a representation of~~ Figures 7A-7J show the nucleotide and corresponding amino acid sequence of murine SEQ ID NOS: 1 and 2, respectively) and human (SEQ ID NOS: 3 and 4, respectively) NR4 (IL-13Rα) genes. The nucleotide and predicted amino acid sequence of human (H) and murine (M) IL-13Rα(NR4) were aligned by eye, with gaps (-) inserted to optimize the alignment. The numbering is for the murine clone,

nucleotides that form part of the coding region are shown in upper case, whilst those of the untranslated regions are shown in lower case. Amino acids identical between the predicted murine and human proteins are indicated by (*). DNA encoding the murine signal sequence is underlined, with A26 or T27 being the predicted first amino acid of the mature protein.

B5

Page 33, beginning at line 12, please amend the paragraph to read as follows:

Figure 10 is a representation of the N-terminal amino acid sequence of murine NR4 (SEQ ID NOS: 10 and 11).

B6

Page 37, beginning at line 3, please amend the paragraph to read as follows:

A library was constructed λZAP II using ApoI digested genomic DNA from embryonal stem cells and screened with a pool of ^{32}P-labelled oligonucleotides encoding the amino acid sequence Trp-Ser-Asp-Trp-Ser (SEQ ID NO: 12) found in many members of the haemopoietin receptor family. One hybridising bacteriophage clone was found to contain a sequence that appeared to encode part of a novel member of the haemopoietin receptor family. This receptor was given the operational n ame NR4. The sequence of the genomic clone was used to isolate cDNAs encoding NR4 from WEHI-3B cell, peritoneal macrophage, bone marrow, skin and kidney libraries. A composite of the nucleotide sequence ([SEQ ID NO: 1]) and predicted amino acid sequence ([SEQ ID NO: 2])of these cDNAs is shown in Figure 1. The NR4 cDNA is predicte4d to encode for a protein of 424 amino acid residues, containing a putative signal sequence and transmembrane domain. The extracellular region of the protein contained an immunoglobulin-like domain (amino acids 27-117), in addition to a typical haemopoietin receptor domain (amino acids 118-340) which includes four conserved cysteine

B7

residues and the characteristic Trp-Ser-Asp-Trp-Ser motif (Figure; in bold as WSXWS). The cytoplasmic tail of the new receptor was 60 amino acids in length.